Remarks/Arguments

Claims 1-27 are pending in the present application. Claims 8, 16 and 24 are canceled; claims 10-24, 26 and 27 are withdrawn from consideration. Accordingly, claims 1-7, 9 and 25 are presented for examination on the merits.

Typographical errors have been corrected in claims 1, 4 and 25. Claim 6 has been amended to provide a functional definition of the claimed ribozyme (page 17, first paragraph). Claim 9 has been amended to recite that there is a bridging sequence between the response elements (Figure 1B). Claims 1 and 25 have been further amended to recite that the claimed ribozyme catalyzes the first TES reaction step in the absence of a guanosine cofactor, and to more particularly define the TES reaction as sequence specific. Support for this amendment is found at page 6, lines 6-8, where it is disclosed that a guanosine cofactor is not required for initiation of the first catalytic step. Accordingly, no new matter is added by these amendments to the claims.

I. Claim Objections

It is respectfully submitted that the amendments to the claims render the objections to claims 1 and 25 moot.

II. Rejection of Claims 1 and 25 Under 35 U.S.C. § 112, Second Paragraph

The examiner objects to the use of the phrase "non-native target RNA sequence, asserting that its use in the claims is contrary to its use in the specification.

Applicants respectfully disagree. Non-native target RMA sequence is defined in the specification at page 5 as sequence within a substrate that is not bound by wild-type ribozymes. The phrase is used in the claims to indicate precisely that. The claimed modified ribozyme recognizes target sequence that is not recognized by wild-type ribozymes. As such, the use of

the phrase is consistent, and its meaning is clear.

Accordingly, the rejection of claims 1 and 25 under 35 U.S.C. § 112, second paragraph is respectfully traversed.

II. Rejection of Claim 4 Under 35 U.S.C. § 112, Second Paragraph

This rejection is rendered moot by the amendment to claim 4.

III. Rejection of Claim 6 Under 35 U.S.C. § 112, Second Paragraph

This rejection is rendered moot by the amendment to claim 6.

IV. Rejection of Claim 8 Under 35 U.S.C. § 112, Second Paragraph

This rejection is rendered moot by the cancellation of claim 8.

V. Rejection of Claim 9 Under 35 U.S.C. § 112, Second Paragraph

This rejection is rendered moot by the amendment to claim 9.

VI. Rejection of Claims 1 and 25 Under 35 U.S.C. § 102(b) Over Sargueil et al.

Claims 1 and 25 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Sargueil et al. The examiner asserts that the cited reference teaches a ribozyme having two recognition elements wherein at least one element is complementary to non-native target RNA.

This rejection is respectfully traversed as follows.

One embodiment of the present invention is directed to a ribozyme that catalyzes a first step TES reaction without a guanosine cofactor. Using only water as the nucleophile, the claimed ribozyme efficiently proceeds through the TES reaction. The claimed ribozyme also contains an internal guide sequence (IGS), which can be modified for interaction with any desired target sequence. That is, the claimed ribozyme contains sequence that is complementary

to, *i.e.*, recognizes and binds to the target sequence through base pairing.

In contrast, Sargueuil discloses a ribozyme that uses guanosine as a required cofactor for the first TES reaction step. Thus, the mechanism of action of the Sargueil ribozyme is different from that of the claimed ribozyme.

Furthermore, Sargueil's ribozyme lacks an IGS (see Sargueil et al., Abstract). Instead, Sargueil's ribozyme recognizes its target based on the fact that the target adopts a particular structure (called a pseudoknot). Although the prior art ribozyme can target different sequences, they are only targeted because they can adopt the pseudoknot structure, not because of any sequence specific interactions. It is mentioned throughout the cited publication that Sarguail's ribozyme only targets particular structures. In fact, because Sargueil's ribozyme lacks an IGS and requires a guanosine cofactor, it is impossible for this prior art ribozyme to carry out the claimed sequence-specific TES reaction.

Accordingly, the rejection of claims 1 and 25 under 35 U.S.C. § 102(b) over Sargueil et al. is respectfully traversed.

VII. Rejection of Claims 1-5 and 25 Under 35 U.S.C. § 103(a)

Claims 1-5 and 25 stand rejected under 35 U.S.C. § 103(a) as unpatentably obvious over Sargueil et al. in view of Harley et al. and Sullenger et al. Sargueil is applied as above. The examiner admits that Sargueil does not disclose that the prior art enzyme can be used to excise specific genetic mutations. Harley is relied on as teaching the mutation associated with muscular dystrophy; and Sullenger is relied on as disclosing a ribozyme that has been modified to carry out the second step of a trans splicing reaction. The examiner concludes therefore, that it would have been obvious to one of skill in the art to modify Sargueil's ribozyme to recognize and splice a sequence associated with a genetic mutation.

Applicant respectfully disagrees with the examiner's conclusion.

As discussed above, Sargueil's ribozyme requires guanosine to carry out the TES reaction. The deficiency of the primary prior art reference is not compensated by either Sullenger or Harley. The latter reference does not address ribozyme activity and Sullenger, like, Sargueil, teaches a ribozyme that initiates self-splicing "by attack of an intron-bound guanosine at the 5' splice site." (fFigure lend to Figure 1 and Figure 1 for a cartoon of the disclosed first step of the ribozyme reaction). Thus, the combined prior art does not disclose or suggest the claimed ribozyme.

Accordingly, the rejection of claims 1-5 and 25 under 35 U.S.C. § 103(a) over sargueil et al., in view of Harley et al and Sullenger et al. is respectfully traversed.

VIII. Rejection of Claims 1-5, 7 and 25 Under 35 U.S.C. § 103(a)

Claims 1-5, 7 and 25 are rejected under 35 U.S.C. § 103(a) as unpatentably obvious over Sargueil et al., in view of Harley et al., Sullenger et al., and further in view of Testa et al. the examiner applies the first three cited references as above and relies on Testa as teaching isolation of a Group I intron structure capable of self-splicing from *P. carinii* rRNA. The examiner asserts that given the teachings of Testa et al. it would have been obvious to one of skill in the art that ribozymes from the same family are functionally equivalent and the choice of one group I ribozyme from one source over another is merely design choice.

As discussed above, Applicant's ribozyme is not functionally equivalent to Sargueil's ribozyme despite the fact that it is a group I ribozyme. Thus, it cannot be considered obvious to substitute applicants' ribozyme for that disclosed in Sargueil et al.

Furthermore, Testa does not disclose or suggest that the ribozyme is capable of being modified to enable trans excision of a non-native target sequence. As such, the combination of cited prior art does not render the claimed invention obvious.

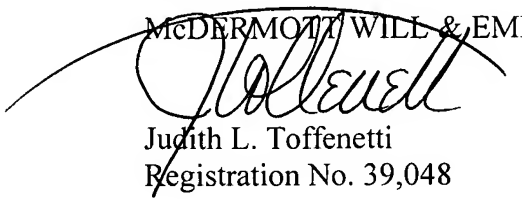
Accordingly, the rejection of claims 1-5, 7 and 25 under 35 U.S.C. § 103(a) over the cited combination of prior art is respectfully traversed.

Is respectfully submitted that the amendments above place the application in condition for allowance, an early notification thereof being earnestly solicited. However, if any issues remain outstanding, the Examiner is respectfully requested to contact the undersigned so the prosecution may be expedited.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

McDERMOTT WILL & EMERY LLP



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